



ANK2 gene

ankyrin 2

Normal Function

The *ANK2* gene provides instructions for making a protein called ankyrin-2. Ankyrin-2 is part of a larger family of ankyrins, which interact with many other types of proteins in cells throughout the body. Ankyrins ensure that certain proteins are inserted into the correct locations in the cell membrane and are anchored to the cell's structural framework (the cytoskeleton). Ankyrins play key roles in important cellular functions including movement, growth, and division.

The ankyrin-2 protein is active in many cell types, particularly in the brain and in heart (cardiac) muscle. This protein mainly targets ion channels, which are complexes of proteins that transport charged atoms (ions) across cell membranes. In the heart, the flow of ions (such as sodium, potassium, and calcium) through ion channels is critical for signaling the heart to beat and for maintaining a normal heart rhythm. Ankyrin-2 inserts these channels into their proper locations in the cell membrane so they can regulate the flow of ions into and out of cardiac muscle cells.

Health Conditions Related to Genetic Changes

Romano-Ward syndrome

At least 10 mutations in the *ANK2* gene have been associated with a variety of heart problems. It is unclear whether these mutations cause Romano-Ward syndrome or lead to another heart condition with some of the same signs and symptoms.

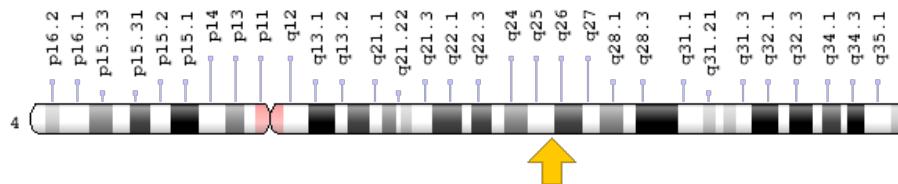
Most often, mutations in the *ANK2* gene lead to abnormalities of the heart's natural pacemaker (the sinoatrial node), a heart rate that is slower than normal (bradycardia), a disruption in the rhythm of the heart's lower chambers (ventricular arrhythmia), and an increased risk of fainting (syncope) and sudden death. Other symptoms, including seizures, dizziness, and migraine headaches, also have been reported in people with *ANK2* mutations.

Each of the identified mutations in the *ANK2* gene changes a single protein building block (amino acid) in a critical region of the ankyrin-2 protein. As a result, the altered protein cannot target ion channels to their correct locations in cardiac muscle cells or other types of cells. Although the channels are produced normally by the cell, they are unable to function if they are not inserted correctly into the cell membrane. This loss of functional channels in the heart disrupts the normal flow of ions, which alters the heart's normal rhythm and probably interferes with other aspects of cardiac function.

Chromosomal Location

Cytogenetic Location: 4q25-q26, which is the long (q) arm of chromosome 4 between positions 25 and 26

Molecular Location: base pairs 112,706,083 to 113,383,740 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ANK2_HUMAN
- ankyrin 2, neuronal
- ankyrin-2, nonerythrocytic
- ankyrin B
- ankyrin, brain
- ankyrin, nonerythroid
- brank-2
- LQT4

Additional Information & Resources

GeneReviews

- Long QT Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1129>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ANK2%5BTIAB%5D%29+OR+%28ankyrin+2,+neuronal%5BTIAB%5D%29%29+OR+%28%28ankyrin+B%5BTIAB%5D%29+OR+%28ankyrin,+brain%5BTIAB%5D%29+OR+%28ankyrin,+nonerythroid%5BTIAB%5D%29+OR+%28ankyrin-2,+nonerythrocytic%5BTIAB%5D%29+OR+%28brank-2%5BTIAB%5D%29+OR+%28LQT4%5BTIAB%5D%29%29+AND+%28Genes%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- ANKYRIN 2
<http://omim.org/entry/106410>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_ANK2.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=ANK2%5Bgene%5D>
- HGNC Gene Family: Ankyrin repeat domain containing
<http://www.genenames.org/cgi-bin/genefamilies/set/403>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=493
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/287>
- UniProt
<http://www.uniprot.org/uniprot/Q01484>

Sources for This Summary

- Chiang CE. Congenital and acquired long QT syndrome. Current concepts and management. *Cardiol Rev.* 2004 Jul-Aug;12(4):222-34. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15191637>
- GeneReview: Long QT Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1129>
- Mohler PJ, Bennett V. Ankyrin-based cardiac arrhythmias: a new class of channelopathies due to loss of cellular targeting. *Curr Opin Cardiol.* 2005 May;20(3):189-93. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15861006>

- Mohler PJ, Gramolini AO, Bennett V. Ankyrins. *J Cell Sci.* 2002 Apr 15;115(Pt 8):1565-6.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11950874>
- Mohler PJ, Schott JJ, Gramolini AO, Dilly KW, Guatimosim S, duBell WH, Song LS, Haurogné K, Kyndt F, Ali ME, Rogers TB, Lederer WJ, Escande D, Le Marec H, Bennett V. Ankyrin-B mutation causes type 4 long-QT cardiac arrhythmia and sudden cardiac death. *Nature.* 2003 Feb 6; 421(6923):634-9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12571597>
- Mohler PJ, Splawski I, Napolitano C, Bottelli G, Sharpe L, Timothy K, Priori SG, Keating MT, Bennett V. A cardiac arrhythmia syndrome caused by loss of ankyrin-B function. *Proc Natl Acad Sci U S A.* 2004 Jun 15;101(24):9137-42. Epub 2004 Jun 3.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15178757>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC428486/>
- Sherman J, Tester DJ, Ackerman MJ. Targeted mutational analysis of ankyrin-B in 541 consecutive, unrelated patients referred for long QT syndrome genetic testing and 200 healthy subjects. *Heart Rhythm.* 2005 Nov;2(11):1218-23.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16253912>

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